"INPHASE OPPOSED PHASE IMAGING OF BONE MARROW DIFFERENTIATING NEOPLASTIC LESIONS FROM NON NEOPLASTIC LESIONS"

Dissertation submitted for

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AND

GOVERNMENT GENERAL HOSPITAL

CHENNAI – 600 003

THE TAMIL NADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI – 600 032

APRIL 2011

“Learn to heal”

CERTIFICATE

This is to certify that **Dr. N.SUNDARESWARAN** has been a post graduate student during the period April 2008 to April 2011 at Barnard Institute of Radiology, Madras Medical College, Government General Hospital, Chennai.

This Dissertation titled **"INPHASE OPPOSED PHASE IMAGING OF BONE MARROW DIFFERENTIATING NEOPLASTIC LESIONS FROM NON NEO PLASTIC LESIONS"** is a bonafide work done by him during the study period and is being submitted to the Tamilnadu Dr. M.G.R. Medical University in partial ful fillment of the M.D. Branch VIII Radiodiagnosis Examination

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DECLARATION

I **Dr.N.SUNDARESWARAN,** solemnly declare that this dissertation entitled, **"INPHASE OPPOSED IMAGING OF BONE MARROW DIFFERENTIATING NEOPLASTIC LESIONS FROM NON NEOPLASTIC LESIONS"** is a bonafide work done by me at the Barnard Institute of Radiology, Madras Medical College and Government General Hospital during the period 2008 – 2010 under the guidance and supervision of the Director, Barnard Institute of Radiology of Madras Medical College and Government General Hospital, Professor **K. Vanitha, M.D., D.M.R.D., D.R.M.,** This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree Radiodiagnosis.**

Place : Chennai

Date: 30.11.10 **Dr. N.SUNDARESWARAN**

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CONTENTS

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L.Dis.No.14597/ME5/Ethics Dean/MMC/2010 Dated : 12.05.2010

Title of the work : "Inphase – Opposed Phased MRI Imaging of Bone Marrow Disorders".

Principal Investigator : Dr. N. Sundareswaran.
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The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 12th May 2010 at 2.p.m in Pharmacology Seminar Hall, Madras Medical College, Chennai -3

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

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2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
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7. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
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INTRODUCTION

MAGNETIC RESONANCE (MR) imaging has become preferred over other imaging modalities in evaluating disease in the bone marrow. The bone marrow represents 5% of body weight and consists of hematopoietic components (40% fat, and 40% water, and 20%protein) and lipomatous components (80% fat, 15% water, 5% protein) with a variable trabecular bone lattice. Bone marrow is a richly vascularised, dynamic and highly responsive system that is prominently targeted in many physiologic and pathologic processes. It is a non invasive technique complements bone marrow aspirations and biopsies by sampling a large volume of bone marrow and by providing information that aids the diagnosis, staging, and follow-up of hematologic malignancies.

Conventionally, bone marrow is examined by means of bone marrow aspiration biopsy or trephinement of the posterior iliac crest. Both techniques provide a localized view of the state of the marrow and may be subject to sampling errors when used in disorders known to affect the marrow focally. An objective and non invasive method of assessing and characterizing bone marrow would be a useful clinical adjunct to bone marrow aspiration and trephinement.

Examination of the bone marrow has traditionally been provided by biopsy or aspiration approaches or by relatively insensitive or non-specific techniques such as scintigraphy, radiography or computed tomography. MR, with its multifaceted imaging and quantitative capabilities, has found wide application in the assessment of the bone marrow, both on a research and clinical basis.

Each of the various MR pulse sequences, ranging from spin-echo(SE), and short TI inversion recovery (STIR) to more advanced chemical shift techniques (opposed phase) offers unique opportunities to detect, assess and quantify the many processes affecting the bone marrow. These processes include age-related marrow conversion and reconversion, hematologic disorders, diffuse and focal neoplastic processes, storage and marrow packing disorders, ischemic and hyperaemic conditions, traumatic and infectious processes, toxic exposures, and metabolic bone disorders such as osteoporosis. The age-related patterns of hemateopoietic tissue regression from the appendicular skeleton and the progressive conversion of marrow in the axial skeleton are well documented.

Variable reconversion patterns, particularly well defined with opposed phase sequences have been observed. Non-neoplastic hematologic conditions, ranging from hemolytic anemia with myeloid hyperplasia and reconversion to aplastic anemia with myeloid depletion, have been widely investigated with various MR techniques. Marrow-based neoplastic processes, both diffuse and focal, have also been extensively studied with MR.

AIM & OBJECTIVES

Neoplastic and non neoplastic lesions in the bone marrow may have similar signal intensity on conventional MR imaging sequences.

(i) Purpose of this study is whether inphase opposed phase imaging can helps to differentiate neoplastic and non neoplastic lesions of bone marrow

(ii) To assess sensitivity and specificity of inphase opposed phase imaging in Differentiating neoplastic and non neoplastic lesions of bone marrow

REVIEW OF LITERATURE

MRI of Bone Marrow

Normal Anatomy

The normal bone marrow has three primary components: osseous matrix, red marrow, and yellow marrow. The osseous components of the marrow are the trabeculae of cancellous bone, which provide the supporting framework for the red and yellow marrow elements. The red or cellular marrow is hematopoietically active,producing RBCs, WBCs, and platelet precursors. Hematopoietically inactive yellow marrow is composed of fat cells. These two types of marrow differ in their chemical composition. Recognition of these differences is important to understanding the MRI appearance of marrow.

In infants and young children, red marrow consists of approximately 40% water, 40% fat, and 20% protein .As the individual ages, the fatty elements of hematopoietic marrow increase, and by age 70 years, red marrow is composed of approximately 60% fat, 30% water, and 10% protein. Yellow marrow contains approximately 80% fat, 15% water, and 5% protein

BONE MARROW PHYSIOLOGY

The bone marrow is the 5th largest organ of the human body. Its chief function is hematopoietic, providing the optimal supply of circulating platelets, white and red blood cells to meet the body´s requirements for coagulation, immunity, and oxygenation.

The histology of normal bone marrow consists of a number of components including: (1) an osseous component; (2) a cellular component; (3) a supporting system. The osseous component consists of cancellous bone composed of primary and secondary trabeculae. The cellular component includes hematopoietic, fat, and reticulum cells. The bone marrow supporting system consists of vascular, neural, and lymphatic celements.

Hematopoietically active bone marrow is referred to as hematopoietic marrow or red marrow. Red marrow contains approximately water,40% fat, and 20% protein. Hematopoietically inactive marrow is referred to as yellow marrow or fatty marrow. It contains approximately 15% water, 80% fat, and 5% protein. These differences in chemical composition account for the appearance of red and yellow marrow on various MRI pulse sequences. There is also a

structural difference between red and yellow marrow. In particular, the vascular network of red marrow can be characterized as being rich, while that of yellow marrow is more sparse.

At birth, red marrow is present throughout the entire skeleton. Epiphyses and apophyses are cartilaginous at birth; however, they later contain yellow marrow throughout life. Epiphyseal red marrow can be a normal variant in adults, however, in the humeral head and femoral head. Normal physiological conversion of red-to yellow marrow occurs in a predictable and orderly fashion with completion by the age of 25 years when the adult pattern is reached.

Conversion occurs first in the hands and feet. There is then a “distal to proximal“ trend of conversion within the bones of the extremities. Conversion also occurs at different rates within the same bone. Within long bones, marrow converts first in the diaphysis, then in the distal metaphysis, and finally in the proximal metaphysis. By age 25 years, the adult distribution of bone marrow is attained which is characterized by red marrow persisting in the axial skeleton, proximal humerus, and proximal femur. With advancing age there is further replacement of red marrow by yellow marrow, with older individuals commonly having a spine and pelvis dominated by yellow marrow.

Residual islands of hematopoietic marrow can persist in the long bones. The most common sites are the proximal and distal femur, and proximal humerus. This pattern should not be mistaken for pathology. Another common normal variation in distribution of marrow is the presence of focal fatty marrow within the spine. The distal appendicular skeleton usually has a uniform distribution of yellow marrow in adults.

MRI Appearance of Normal Marrow

The MR appearance of the bone marrow depends on the pulse sequence selection and the relative amounts of cellularity, protein, water, and fat within the marrow. Spin-echo and fat-suppressed sequences have been most widely used to image bone marrow. The addition of other sequences will be influenced by the disease process and anatomic region being evaluated.T1-weighted spin-echo sequences allow superb differentiation between red and yellow marrow.

On T1-weighted images, hematopoietic marrow usually shows a signal intensity equal to or slightly higher than that of muscle on both T1- and T2- weighted sequences. In neonates, the signal intensity of hematopoietic marrow may be slightly lower than that of muscle on T1-weighted images, reflecting the larger percentage of cellular

marrow. After the neonate period, signal intensity lower than normal muscle almost always indicates pathology. Yellow marrow is isointense with subcutaneous marrow onT1-weighted spin-echo sequences. On T2-weighted spin-echo sequences, the signal intensity of fatty marrow is usually higher than that of muscle and equal to or slightly lower than that of subcutaneous fat.

Contrast differences between normal and pathologic marrow and between red and yellow marrow on T2-weighted images can be accentuated by using fat-suppressed sequences, either the fat-saturation technique or STIR images[13].On these sequences, hematopoietic marrow shows intermediate signal intensity similar to that of muscle, whereas fatty marrow shows a signal intensity lower than that of muscle. By comparison, most marrow pathology exhibits relatively high signal intensity, greater than that of red and yellow marrow, on fat-suppressed images. The use of contrast-enhanced MRI can also improve lesion conspicuity. Normal marrow shows minimal enhancement after administration of gadolinium chelate agents. By comparison, many malignant neoplasms exhibit an increasing signal intensity that is greater than the increase shown by normal marrow and by benign lesions[14].

Distribution of Normal Marrow

The ability to recognize the normal variations in bone marrow distribution is important so that they are not interpreted as abnormal. Bone marrow is a dynamic organ that changes composition throughout life (Fig1)[3,4,15,16.] At birth, the marrow contains a predominance of hematopoietically active cells. Shortly after birth, an orderly and predictable conversion of hematopoietic to fatty marrow takes place, which begins in the appendicular or peripheral skeleton and progresses to the axial or central skeleton. Within individual long bones, marrow conversion occurs first in the diaphysis, then in the distal metaphyses, and finally in the proximal metaphyses. The adult pattern of marrow distribution is reached by the middle of the third decade. At this time, red marrow is predominantly seen in the axial skeleton (skull, spine, sternum, flat bones) and the proximal ends of the humerus and femurs; yellow marrow predominates in the remainder of the long bones and the epiphyses and apophyses(Fig2) [15,22 ·] islands of red marrow can also be seen in the distal ends of the femurs in marathon runners and menstruating women.

One common exception to the normal pattern of complete conversion is the epiphyses. The epiphyses are cartilaginous before they ossify. Cartilaginous epiphyses and apophyses exhibit signal intensity equal to that of muscle on T1-weighted images and equal to or slightly

higher than that of fat on T2-weighted images. Once ossification has been present for 3 to 4 months, the epiphyses and apophyses exhibit high signal intensity on both T1- and T2-weighted images, reflecting their predominantly fatty marrow. How-ever, islands of low-signal-intensity red marrow can be seen within the subchondral regions of the proximal humeral epiphyses on T1-weighted images in healthy adolescents and adults[23] .

Age-related changes in marrow conversion have also been addressed in the axial skeleton. In the first decade of life, the vertebral marrow is predominantly hematopoietic and shows homogeneously low signal intensity except for high signal intensity around the basivertebral vein. With aging, the amount of hematopoietic marrow in the vertebral bodies progressively decreases, but even in adults the vertebral bodies contain abundant red marrow. The decline in red marrow is accompanied by an increase in fatty marrow. In the first decade of life, the signal intensity of the vertebral bodies is often lower than that of the adjacent disk space. In individuals older than 10 years, the signal intensity of the vertebral marrow is higher than that of the adjacent disk. The conversion of red to yellow marrow in the vertebral bodies can occur in a diffuse or focal pattern [19].

An age related pattern of red to yellow marrow conversion also occurs in the pelvis. Pelvic marrow is pre dominantly hematopoietic in the first two decades of life [17]. Red to yellow conversion begins in the acetabulum superiorly and medially. By the third decade, these areas usually contain mainly fatty marrow.

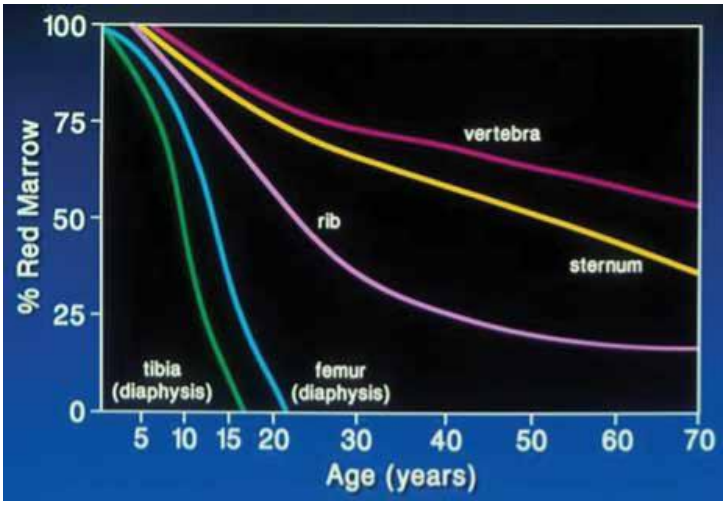


Fig 1.Normal conversion of hematopoietic marrow into fatty marrow from birth to 70 years. Diagram shows percentages of hematopoietic marrow at different anatomic sites. Conversion of red to yellow marrow occurs earlier in appendicular than in axial skeleton

Fig 2. Normal distribution pattern of adult marrow. Hematopoietic marrow (*in red*) resides in skull, vertebral bodies, flat bones, and proximal femoral and humeral metaphyses. Fatty marrow (*in yellow*) predominates in remainder of skeleton

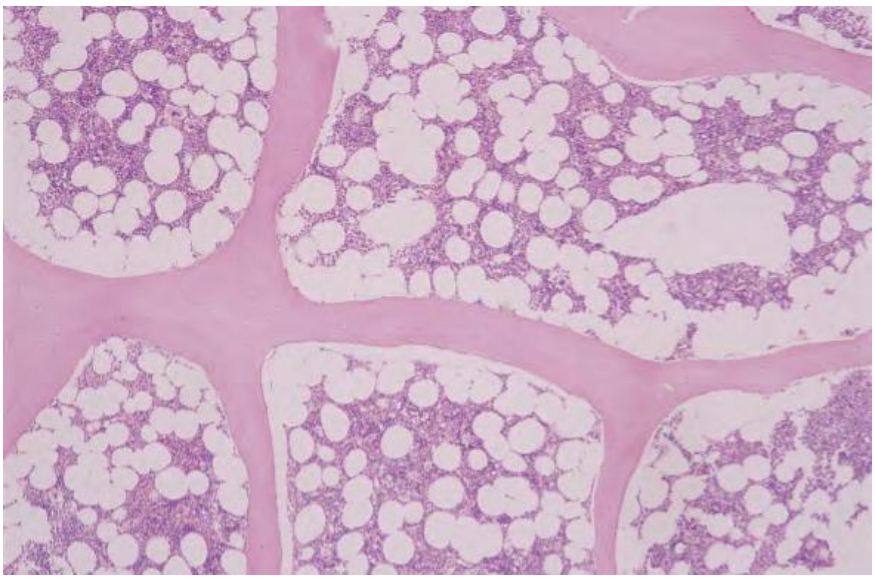


Fig 3.BM trephine biopsy sectionshowing normal bone structure; there are anastomosing bonytrabeculae. Paraffi n - embedded, H & E× 5.

Classification of bone marrow disorder:

Disorders that affect marrow production can be divided into four categories:

1. Marrow reconversion or hyperplasia,

2. Marrow infiltration disorders,

3. Myeloid depletion disorders (hypo cellular or fatty marrow)

4. Myelofibrosis

Others like bone marrow ischemia (avascular necrosis, medullary infarct), bone marrow edema

1. Marrow Reconversion (Myeloid Hyperplasia):

Marrow reconversion refers to the repopulating of yellow marrow by hematopoietic cells. Fatty marrow reconverts to red marrow where there is an increased demand for Haematopoiesis and the hematopoietic capacity of existing red marrow stores is exceeded. Reconversion occurs in a pattern opposite that of physiologic marrow conversion, beginning in the vertebrae and flat bones of the pelvis and then progressing to the long bones of the extremities and ultimately to the hands and feet. In

the individual long bones, marrow reconversion first occurs in the proximal metaphyses, followed by the distal metaphyses, and the diaphysis. Reconversion occurs in the epiphyses and apophyses only when severe hematopoietic stress is present.

Causes of reconversion include

i) Severe chronic anaemia(such as sickle cell disease, thalassemia, or hereditary spherocytosis),

ii) Treatment with granulocyte-macrophage colony-stimulating factor (GMCSF) during chemotherapy,

iii) Circumstances in which an increased oxygen requirement is present (e.g., rigorous athletics such as marathon running and high altitudes)

2.Marrow Replacement Disorders:

Marrow can be replaced or infiltrated by number of disorders, Including leukemia, lymphoma, multiple myeloma, and metastases. Diseases such as leukemia, lymphoma, and multiple myeloma tend to originate in the hematopoietic marrow. Metastases localize in the red marrow because it has a richer blood supply than fatty marrow. In adult patients, the common sites for metastatic disease are the

vertebrae (69%), pelvis (41%), proximal femoral metaphyses (25%), and skull (14%)

3. Myeloid Depletion:

Myeloid depletion refers to the loss of normal red marrow. Pathologically, the marrow is acellular or hypo cellular, with yellow marrow filling the marrow space.

Causes of myeloid depletion include

i) Viral infections,

ii) Medications,

iii) Chemotherapy

iv) Radiation therapy,

But in many instances, the cause is unknown. Aplastic or hypo plastic marrow shows diffusely high signal intensity on both T1- and T2-weighted images and low signal on fat-suppressed images [30,31] . The increase in fatty marrow is best appreciated in areas that normally contain a predominance of red marrow, such as the spine and pelvis. Radiation is a cause of focal marrow depletion. Radiation induced changes have been most often described in the spine[32,34] Initial pathologic changes include edema, vascular congestion, and diminished

haematopoiesis. The marrow subsequently is replaced by fat and fibrosis. These changes are usually complete by 3 months after the start of therapy. Alterations in marrow signal intensity can be observed as early as 2 weeks after initiation of treatment, especially on STIR images. The early pattern is that of low signal intensity on T1-weighted images and high signal intensity on T2-weighted and fat-suppressed sequences. The later pattern of fatty replacement usually appears as homogeneous high signal intensity within the radiation port on T1- weighted images. Fatty replacement also can be noted in non radiated vertebral marrow adjacent to the radiation port in approximately 50% of patients. Decreased contrast enhancement of the nonirradiated bone marrow during and after the end of radiation has been reported on dynamic MRI and is thought to reflect the effect of radiation on the microvasculature of marrow [35.]

Most patients have some degree of hematopoietic marrow recovery within 1 to 2years after radiation therapy. Chemotherapy also results in initial ablation of hematopoietic cells and marrow replacement by edema. Changes in the first few days after the administration of chemotherapy include decreased signal intensity on T1-weighted images and increased signal intensity on T2-weighted and

fat-suppressed sequences. After the initial changes subside, the marrow may repopulate with normal elements or the cellular elements may be replaced by fat or a combination of fat and fibrosis.

4. Myelofibrosis:

Myelofibrosis is characterized by replacement of normal marrow cells by fibrotic tissue. It usually is the result of radiation therapy or chemotherapy, but on occasion it can be a primary disorder. Fibrotic marrow usually produces low signal intensity on both T1- and T2-weighted images.

The signal intensity may be slightly higher than that of muscle on fat-suppressed images. Differential considerations for hypo intense signal intensity include Gaucher's disease and hemosiderosis. Gaucher's disease is an autosomal recessive disease characterized by decreased levels of the enzyme glucocerebrosidase, leading to accumulation of glucocerebrosides within histiocytes in the monocyte-macrophage system. Marrow disease usually follows the distribution of reconverted marrow and begins in the spine, pelvis, and proximal femoral metaphyses. Within the long bones, it progresses from a proxi-mal to distal distribution. Epiphyseal marrow is rarely involved unless

extensive disease is present [36].Hemosiderin deposition can occur secondary to the breakdown of RBCs in haemolytic anemias or as a sequela of chronic blood transfusions [37]. The magnetic susceptibility effects of hemosiderin produce hypointense marrow on all pulse sequences. The marrow signal intensity is usually lower than that of normal hematopoietic marrow. Low signal intensity also can be seen in the liver and spleen.

Marrow Ischemia:

This category of bone marrow disease encompasses both avascular necrosis of subchondral bone and medullary bone infarcts. Bone marrow ischemia favours fatty marrow over hematopoietic marrow. This is most likely due to the limited vascular supply of yellow marrow relative to red marrow.

Marrow Edema

Bone marrow edema is usually focal. There is a nonspecific increase in water content within the bone marrow which manifests decreased signal intensity on T1 weighed spin-echo images, and markedly increased signal intensity on STIR images and T2weighted fast spin-echo images with fat saturation. T2* weighted images are

frequently less sensitive in detecting bone marrow edema due to obscuration of the high signal from the edema by magnetic susceptibility “blooming“ of trabeculae. The finding of bone marrow edema is non specific ,and can be seen as a result of trauma, infection, ischemia, reaction to adjacent neoplasia, or it may be idiopathic. For example, the bone marrow edema seen on MR images of the hip may be secondary to transient or migratory osteoporosis, early osteonecrosis, or the bone marrow edema syndrome.

MR SEQUENCES:

Pulse sequence selection determines the MR appearance of normal bone marrow as well as the sensitivity and specificity for evaluating bone marrow disorders. A highly effective combination of pulse sequences for the evaluation of bone marrow pathology includes:

(1) T1 weighted spin-echo;

(2) fat-saturation T2 weighted fast spin-echo;

(3) STIR/FastSTIR

(4) opposed phase image.

T1 weighted spin-echo

There is superb differentiation between red and yellow bone marrow on T1 weighted spin-echo images. On T1 weighted images the yellow marrow is hyperintense in signal intensity as contrasted with the relatively decreased signal intensity of red marrow. These differences in signal intensity are a direct reflection of the differences in fat/water content within red and yellow marrow. Specifically, increased fat content within yellow marrow contributes to significant shortening of the T1 relaxation time compared with red marrow. Both benign and malignant disorders of bone marrow have long T1 values which result in marrow signal intensity that is significantly decreased. The signal intensity of these lesions on T1 weighted spin-echo images is usually less than that of inter vertebral discs in the spine and less than that of muscle in the extremities.

T2 weighted fast spin-echo and STIR

The clinical advantages of STIR are due to the following characteristics:

(1) Additive T1 and T2 contrast; (2) marked fat suppression; (3) a two-fold increase in the magnetization range of spin-echo sequences. As

a result, STIR images demonstrate extraordinarily high contrast, conspicuousness, and sensitivity for the depiction of most types of bone marrow pathology. The obvious drawbacks of this pulse sequence, however, include relatively long imaging times, and allow signal-to-noise ratio. Conventional intermediate weighted and T2 weighted spin-echo sequences demonstrate relatively low contrast between red marrow and yellow marrow. In addition there is decreased sensitivity and conspicuousness for the depiction of most types of bone marrow pathology. These problems are corrected by utilizing the very long TR and TE times of heavily T2weighted fast spin-echo images used in conjunction with fat saturation. The sensitivity of this sequence for detecting bone marrow pathology is similar to that of STIR imaging. Several practical advantages compared with STIR include: (1)significantly decreased imaging time; (2) improved signal-to-noise ratio. The major disadvantage of T2 weighted fast spin-echo with fat saturation is its dependence on excellent magnetic field homogeneity for adequate fat suppression. Optimal results with fat saturation usually require high-field strength systems, whereas STIR images can be obtained on low-or high field strength systems. The fast inversion recovery techniques significantly reduce the imaging time required for STIR-like images. The role of these techniques in the evaluation of bone

marrow pathology is currently evolving. Recent studies suggest an emerging role for this pulse sequence for performing whole body bone marrow MRI for the evaluation of patients with suspected skeletal metastasis or multiple myeloma.

Opposed phase image

Opposed-phase GRE sequences with a long repetition time have recently been shown to be sensitive for demonstrating red bone marrow pathology. This type of sequence results in low signal intensity of intact redbone marrow and high signal intensity positive contrast imaging of pathology.

Several studies have illustrated the potential use of MR in bone marrow imaging. MR imaging is sensitive in the detection of areas of abnormal marrow. But most neoplastic and non-neoplastic lesions in the bone marrow may have similar signal intensity on conventional MR imaging sequences.

Only few studies have illustrated the use of in phase opposed imaging in bone marrow.

Disler et al.[38]**-**Thirty consecutive patients with 31 suspected bone marrow lesions underwent MR imaging, including two spoiled gradient-echo sequences identical in all parameters except TE which was chosen

such that fat and water were either in phase or out of phase. Relative ratios of the abnormal bone marrow signal intensity and a control site on the in-phase and out-of-phase images were expressed. The images were also assessed independently by two reviewers who were unaware of the patients identities and clinical histories. Reviewers assessed decreased marrow signal intensity relative to control sites on the out-of-phase and in-phase images. Pathologic confirmation was obtained in 16 patients (17 lesions): the remainder of patients had either established diagnoses or determination of benignity based on stability of findings at I year. Relative ratios were compared with the Student's *t* test and receiver operating characteristic (ROC) curve analysis and the reviewers' scores were evaluated with ROC curve analysis. The relative signal-intensity ratios were I .03 ± 0. 13 for the neoplastic group and 0.62 ± 0.13 for the non-neoplastic group ($p < .0001$). ROC curve analysis of the signal-intensity ratios showed z-score of 0.99. A ratio cut off value of 0.81 resulted in 95% sensitivity and 95% specificity for detection of neoplasm. Both reviewers achieved 100% sensitivity and 94-100% specificity for detection of neoplasms. In-phase and out-of-phase gradient-echo MR imaging of bone marrow signal- intensity abnormalities can help predict the likelihood of neoplastic or non-neoplastic lesions.

One group of lesions absent from **Disler et al** study was osteomyelitis, which we would expect to exhibit a range of relative signal-intensity ratios, depending on the degree of infiltration of marrow by inflammatory cellular elements and on whether abscess formation occurred.

Erly WK, Oh ES, Outwater EKet al [39]- Twenty-five consecutive patients who were evaluated for suspected malignancy (lymphoma [4 patients], breast cancer [3], multiple myeloma [2], melanoma [2], prostate [2], and renal cell carcinoma [1] or for trauma to the thoracic or lumbar spine were entered into this study. An 18-month clinical follow-up was performed. Patients underwent standard MR imaging with an additional sagittal in-phase (repetition time [TR], 90–185; echo time [TE], 2.4 or 6.5; flip angle, 90°) and opposed-phase gradient recalled-echo sequence (TR, 90–185, TE, 4.6–4.7, flip angle, 90°). Areas that were of abnormal signal intensity on the T1 and T2 sequences were identified on the in-phase/opposed-phase sequences. An elliptical region of interest measurement of the signal intensity was made on the abnormal region on the in-phase as well as on the opposed-phase images. A computation of the signal intensity ratio (SIR) in the abnormal marrow on the opposed-phase to signal intensity measured on the in-phase images was made. Twenty-one patients had 49 vertebral lesions, consisting of 20 malignant and 29 benign fractures. There was a

significant difference ($P < 0.001$, Student *t* test) in the mean SIR for the benign lesions (mean, 0.58; SD, 0.02) compared with the malignant lesions (mean, 0.98; SD, 0.095). If a SIR of 0.80 as a cut-off is chosen, with >0.8 defined as malignant and <0.8 defined as a benign result, in-phase/opposed-phase imaging correctly identified 19 of 20 malignant lesions and 26 of 29 benign lesions (sensitivity 0.95; specificity, 0.89). There is significant difference in signal intensity between benign compression fractures and malignancy on in-phase/opposed-phase MR imaging. Conversely, based on the current data, it is clear that some benign fractures do not contain sufficient fat to suppress on the opposed-phase sequences. The evolution of the signal intensity changes in benign compression fractures over time with this technique is not known. It may be that the number of false-positives for malignancy of this technique may be reduced when used within a specified time period after the occurrence of a fracture.

MATERIAL AND METHODS:

Study design: prospective study

Study period: May 2008 to May2010

Subjects:

The study population consisted of 38 consecutive patients with suspected bone marrow lesions between the years May 2008 to May 2010 included in the study. The study group consisted of 22 male and 16 female patients, between the age of 11 to 70 years (with a mean age of 40 years). For 26 patients pathological confirmations obtained. Subjects are followed up for a period of 1 year.

The study was approved by the ethical committee and lasted for 24 months.

Inclusion criteria:

- Patients with T1 hypo intense ,T2 hyper intense lesion in the bone marrow MRI
- Fracture less than 10 days only included

Exclusion criteria

- Patients with post surgical changes were excluded from the study.
- Fracture more than 10 days
- Patients with Pacemaker & Metallic Implants.
- Claustrophobic patients.

Patient preparation

- No specific preparation

Methods:

MR Imaging protocol:

All patients were studied with 1.5-T MR imaging units (Seimens machine).

Various standard imaging sequences were routinely used, including

1. T1(TR 400-600, TE 10-20)
2. T2(TR3000- 4000, TE 80- 120)
3. STIR (TR 4000-6000, TE60-100, IT 100-150msec)

Field of view, matrix size, slice thickness and interslice gap were tailored to the specific site under study. Choice of coils was also dependent on the specific anatomic site under study. In addition to the routine sequences all the enrolled patients underwent imaging with two fast multiplanar spoiled gradient-echo sequences.

1.Inphase(TR 100 -120 ,TE4.6 -4.8 msec)

2.Opposed phase(TR 100-120, TE 2.4 -2.6 or 7.2)

Which was selected to image lipid and water spins in phase(4.6 to 4.8 msec) or opposed phase (2.4-2.6 msec or 7.2msec). Ideally the TE on the opposed-phase images would be 2. 1 msec (with fat and water spins directly opposed): however TE ranged between 2.4 and 2.9msec in 18 patients because of inherent gradient limitations imposed by the selection of the other imaging parameters. Also, because of gradient limitations, an opposed phase TE of 2.4-2.9 msec could not be selected in 12 patients and thus an opposed phase TE of 7.2 msec was chosen for these patients. Although a TE as short as possible should be chosen to minimize signal-intensity differences due to T2*effects, these effects would likely be small with the short TEs used in the study. TR ranged from 100 to120 msec. Other imaging parameters included 256 x 192 matrix and a 32-kHz bandwidth.

IMAGE ANALYSIS:

Circular regions of interest as large as possible to include only the abnormal marrow signal intensity under study were selected, identical in location on the in-phase and opposed-phase images and the signal intensity values were recorded. In addition to the foci of abnormal bone marrow signal intensity. Signal intensity in normal-appearing hematopoietic bone marrow (if present) and a skeletal muscle. bladder cavity or saline-phantom control site were recorded. Control sites were chosen as homogeneous tissues containing little or no mixed water and fat, which should not experience loss of signal on the opposed phase images due to opposed lipid and water spins. Signal-intensity ratios were expressed for the in-phase images and the opposed-phase images as signal-intensity ratio= normal or abnormal bone marrow signal-intensity /control signal intensity (muscle. urine [in bladder, or saline phantom).

Relative signal-intensity ratios were then expressed for comparison of the opposed-phase ratios with the in-phase ratios as

$$\text{Relative signal-intensity ratio} = \frac{\text{Signal-intensity ratio of opposed phase image}}{\text{Signal-intensity ratio of in phase image}}$$

to determine if a change occurred in the signal intensity of the lesion with opposed phase imaging. A decrease in signal intensity was considered indicative of both lipid and water protons within the lesion.

The opposed phase and in-phase images for each patient were then reviewed independently by two radiologists. who were experienced in musculoskeletal MR imaging and were unaware of patient identity and clinical information, to visually determine if the signal intensity of the lesion relative to the control site decreased on the opposed phase images compared with the in phase images. Each radiologist graded each patient's images on a five-point scale of confidence for identification of decreased signal intensity in the lesion as follows:

grade 1**.** Definitely no decrease in signal intensity in the lesion relative to the control site on opposed phase images:

grade 2, probably no decrease in signal intensity in the lesion relative to the control site on opposed phase images;

grade3, indeterminate;

grade 4, probably a decrease in signal intensity in the lesion relative to the control site on opposed phase images;

grade *5*, definitely a decrease in signal intensity in the lesion relative to the control site on out-of-phase images. The two radiologists then reviewed the images together and gave each patient a consensus grade.

26 patients (26 lesions) underwent biopsy or definitive surgery subsequent to MR imaging.and their lesions were categorized as neo-plastic or nonneoplastic.

Of the remaining 12 were designated nonneoplastic on the basis of resolution of symptoms , imaging findings after at least 1 year , the basis of MR imaging findings diagnostic of avascular necrosis of bone and stability of findings at 1 year.

OBSERVATION &RESULTS:

Relative Signal intensity ratio (Relative SIR) calculated for all 38 patients

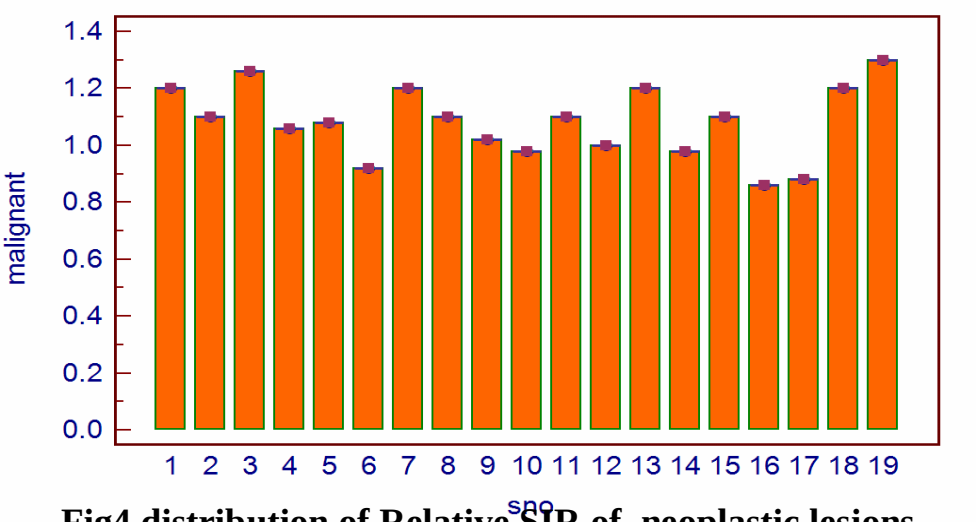


Fig4 distribution of Relative SIR of neoplastic lesions

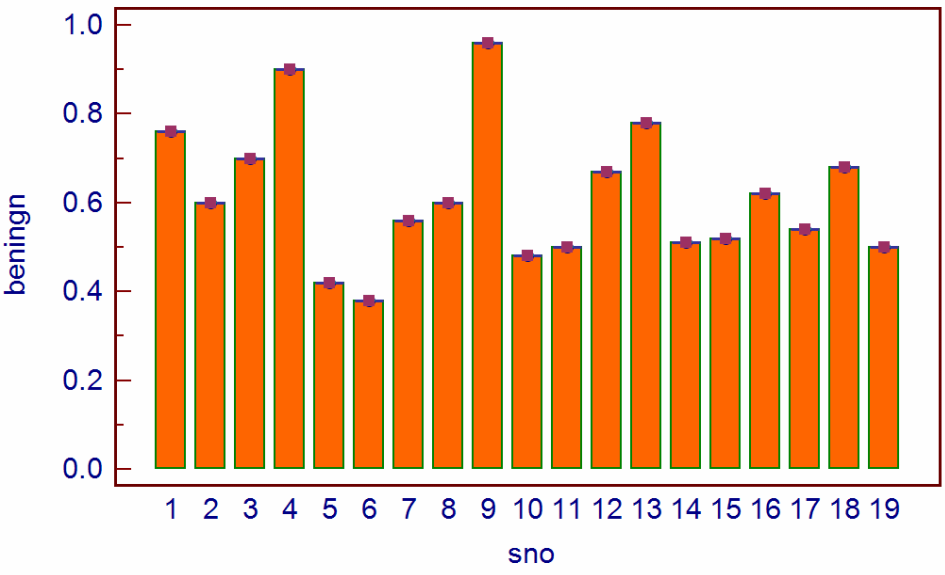


Fig 5. distribution of Relative SIR of non neoplastic lesions

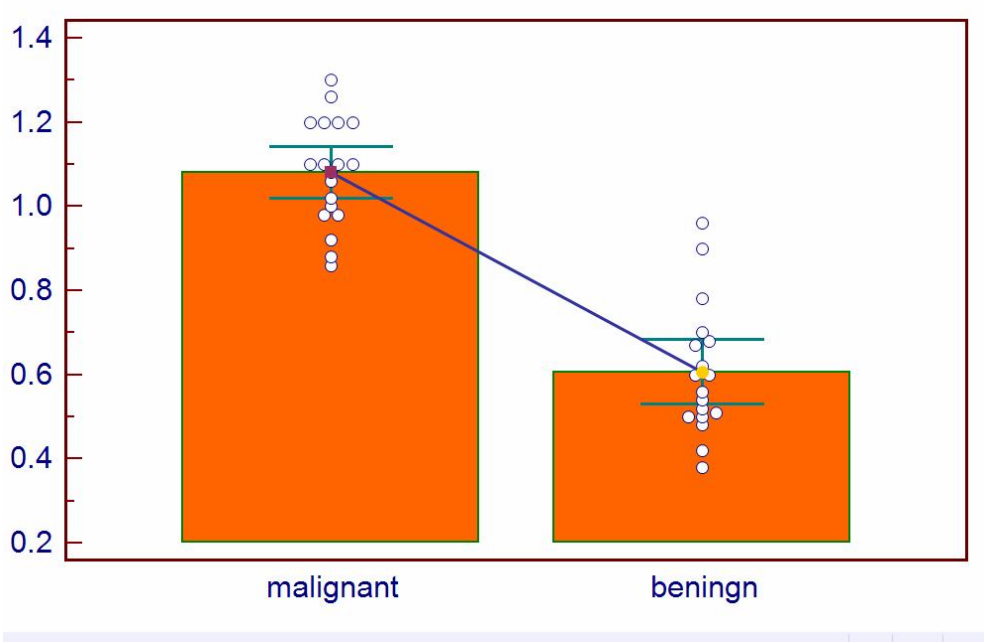


Fig 6.Data comparison graph shows mean difference between the benign and malignant lesion

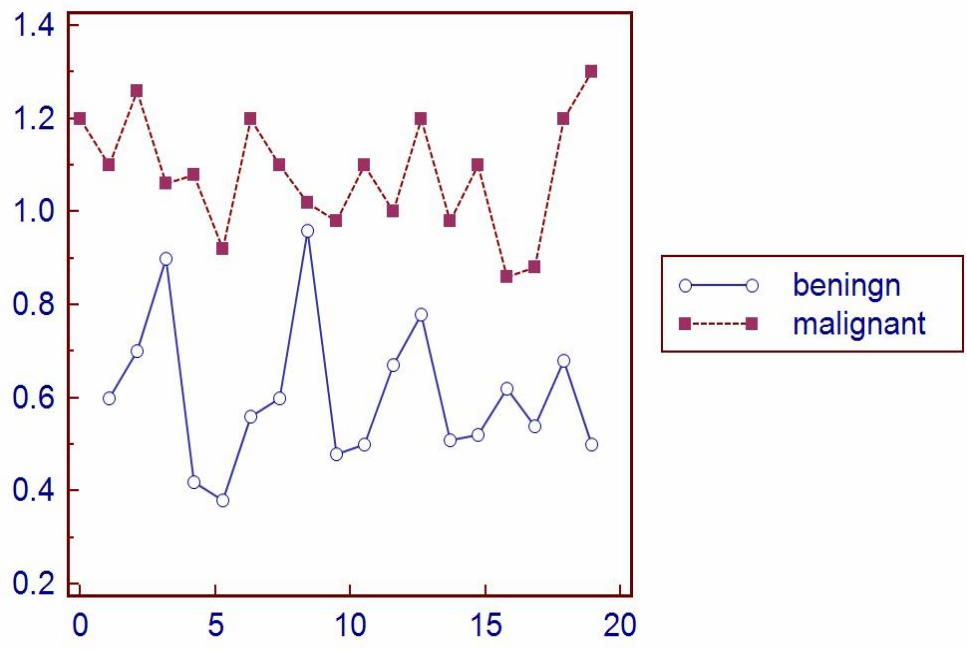


Fig 7. Comparison of relative SIR of malignant and benign lesions

STATISTICAL ANALYSIS:

Statistical analysis were performed with a statistical software system (SPSS Version 17.0 [SPSS] for Windows [Microsoft]

Results were analyzed by following statistical methods

1. Students T test

2. Chi-square test

3. ROC analysis

T-Test:

Group Statistics

	Bone marrow	N	Mean	Std deviation	Std. Error Mean	P value
Relative SIR	**Malignant**	**19**	**1.081**	**0.1257**	**0.0288**	**< 0.001****
	Benign	**19**	**0.615**	**0.1546**	**0.0355**	

P value0.001** means test is <1% level significant

Independent Samples Test:

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Relative SIR	10.202	36	.000	.466	.0457	.3736	.5590
	10.202	34.563	.000	.466	.0457	.3735	.5591

Crosstabs

Bonemarrow Disorders * Relative SIR Crosstabulation

			Relative SIR		Total
			Positive	Negative	
Bone marrow Disorders	Malignant	Count	19	0	19
		% within Bonemarrow Disorders	100%	0%	100.0%
		% within Relative SIR	90.5%	0%	50.0%
	Benign	Count	2	17	19
		% within Bonemarrow Disorders	10.5%	89.5%	100.0%
		% within Relative SIR	9.5%	100%	50.0%
Total		Count	21	17	38
		% within Bonemarrow Disorders	55.3%	44.7%	100.0%
		% within Relative SIR	100.0%	100.0%	100.0%

Chi-Square Tests:

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	30.762(b)	1	.000		
Continuity Correction(a)	27.249	1	.000		
Likelihood Ratio	39.471	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	29.952	1	.000		
N of Valid ases	38				

a Computed only for a 2x2 table b 0 cells (.0%) have expected count less than 5. The minimum expected count is 8.50.

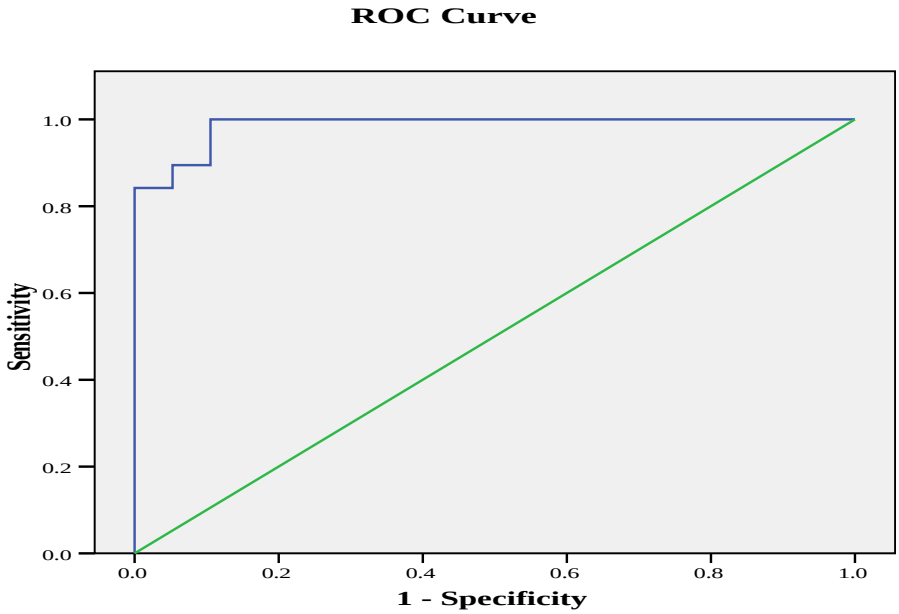
ROC Curve

Case Processing Summary

Bone marrow Disorders	Valid N (list wise)
Positive(a)	19
Negative	19

Larger values of the test result variable(s) indicate stronger evidence for a positive actual state. a The positive actual state is malignant

Area Under the Curve



Test Result Variable(s): Relative SIR

Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
0.986	0.013	0.000	0.960	1.012

a Under the nonparametric assumption

b Null hypothesis: true area = 0.5

Coordinates of the Curve

Test Result Variable(s): Relative SIR

Positive if Greater Than or Equal to (a)	Sensitivity	1 - Specificity
-.620	1.000	1.000
.400	1.000	.947
.450	1.000	.895
.490	1.000	.842
.505	1.000	.737
.515	1.000	.684
.530	1.000	.632
.550	1.000	.579
.580	1.000	.526
.610	1.000	.421
.645	1.000	.368
.675	1.000	.316
.690	1.000	.263
.730	1.000	.211
.770	1.000	.158
.820	1.000	.105
.870	.947	.105
.890	.895	.105
.910	.895	.053
.940	.842	.053
.970	.842	.000
.990	.737	.000
1.010	.684	.000
1.040	.632	.000
1.070	.579	.000
1.090	.526	.000
1.150	.316	.000
1.230	.105	.000
1.280	.053	.000
2.300	.000	.000

a The smallest cut off value is the minimum observed test value minus 1, and the largest cut off value is the maximum observed test value plus1.

In ROC curve If **0.82** as taken as cut off, test shows 100%sensitivity,89.5%specificity. .

Visual interpretation also obtained same results

If 0.82 as taken as cut off value

	MALIGNANT	**BENINGN**
POSITIVE	19	2
NEGATIVE	0	17
	19	19

Sensitivity 100%

Specificity 89.5%

positive predictive value 90%

negative predictive value 100%

Statistical analysis also shows the test highly significant with the P Value <0.0001

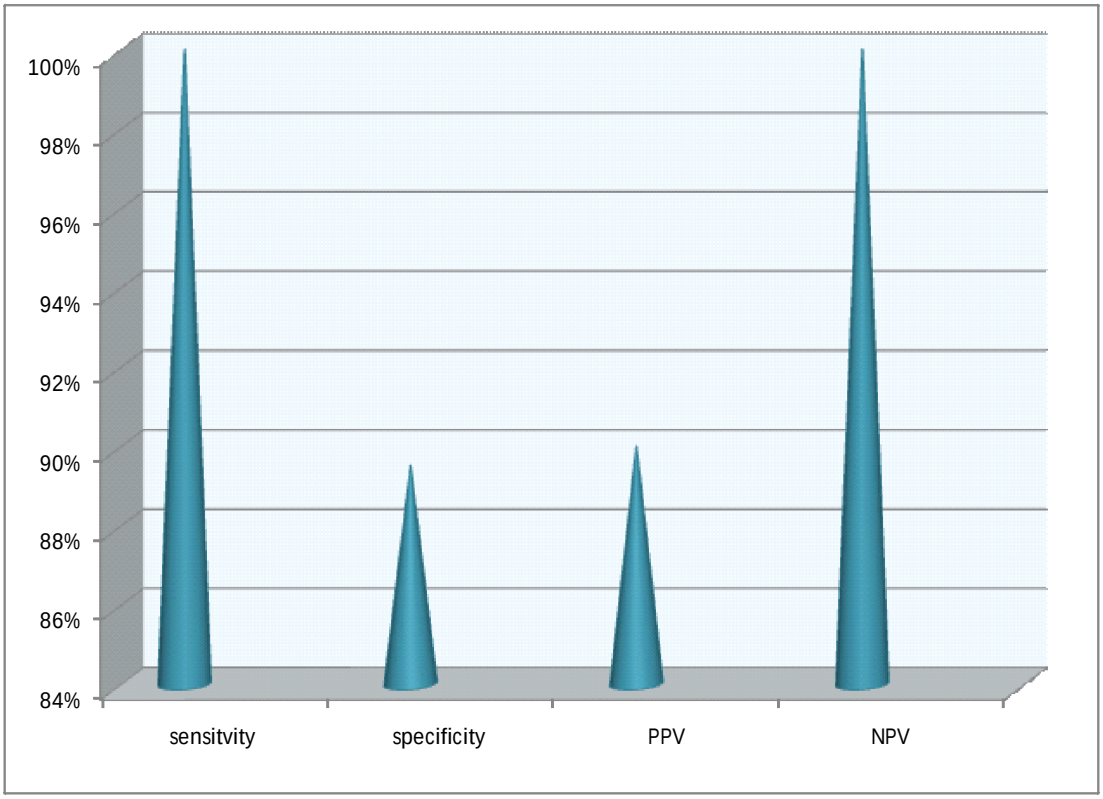


Fig 8 Comparison of sensitivity, specificity, PPV and NPV

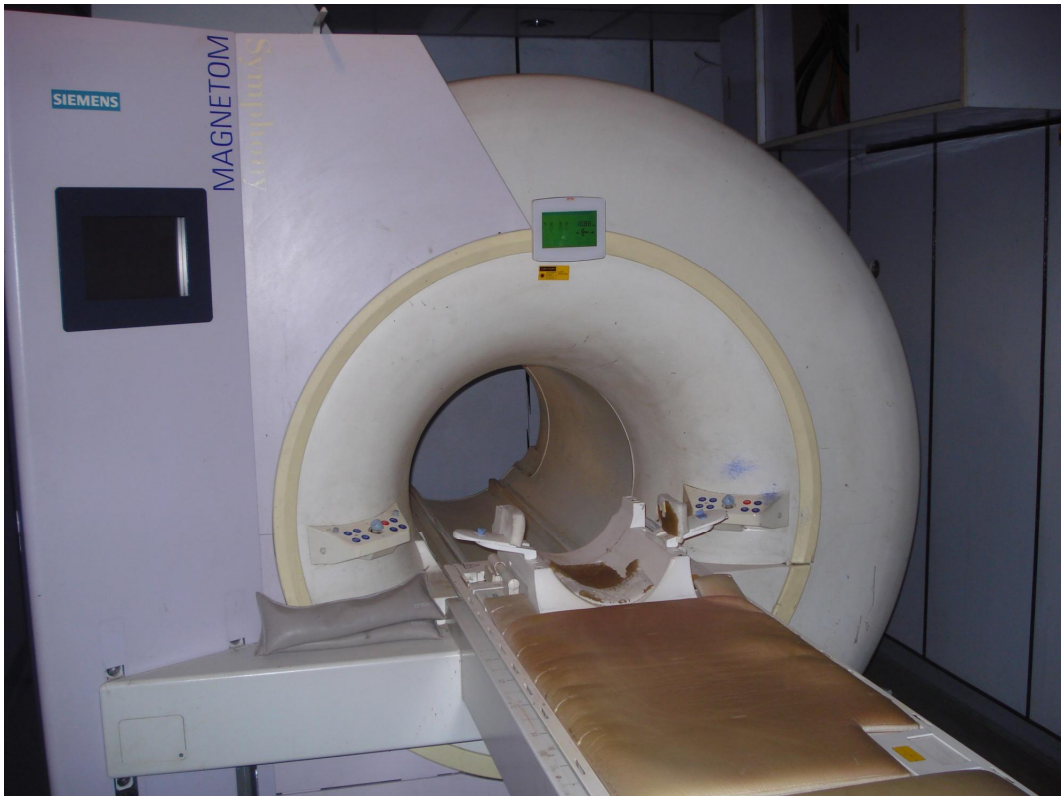


Fig 9. 1.5 Tesla seimens machine used for this study

Fig 10. Method of signal intensity ratio calculation in inphase image

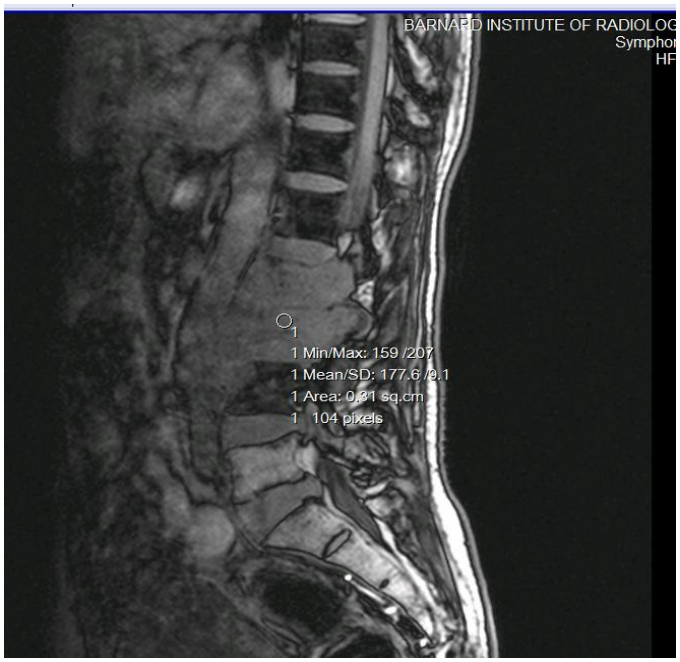


Fig 11.method of signal intensity ratio calculation
in opposed phase image

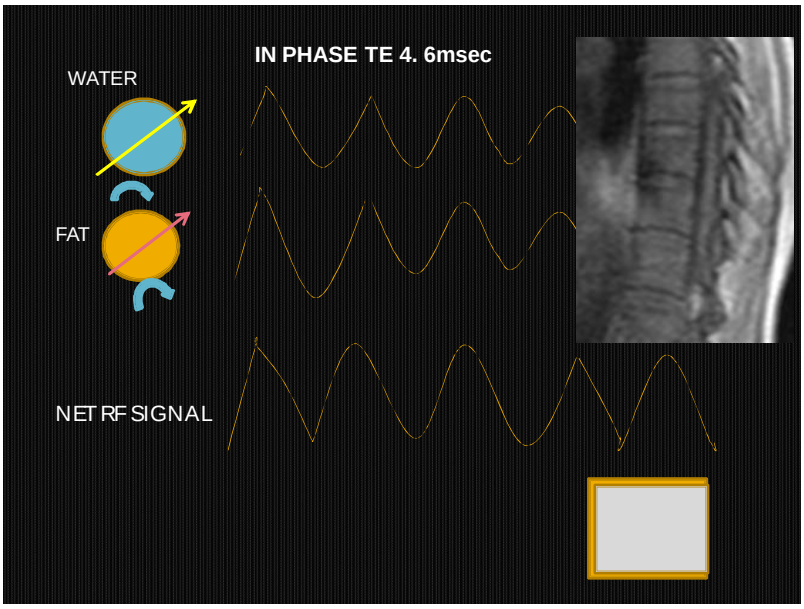


Fig12.illustration of the physical principles of in-phase imaging.
At echo time (TE) of 4.6 ms, both the fat and water protons are in phase, and signal intensity is received from voxels containing both tissue types.

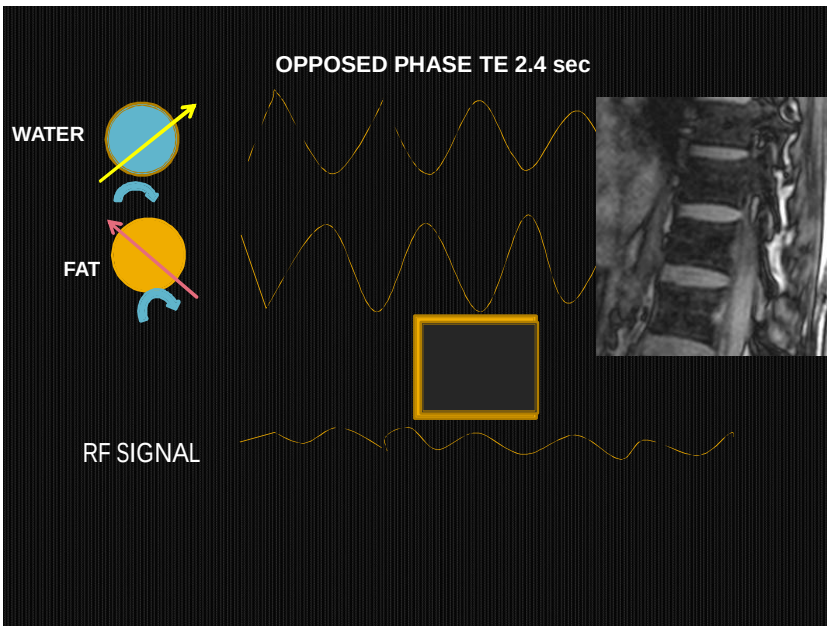


Fig 13 illustration of the physical principles of opposed phase imaging At TE of 2.4 ms, the protons on water and fat molecules are 180°
opposed, and the signal intensity from one cancels the signal intensity from the other. Voxels that contain both tissue types have a reduction in signal intensity.

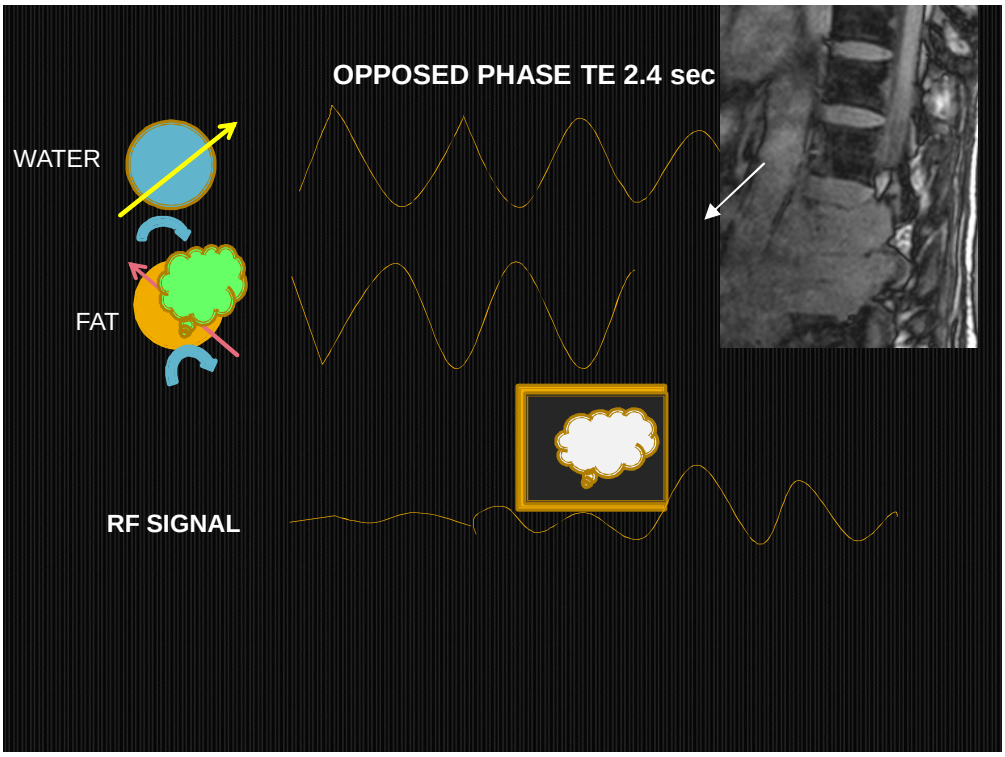


Fig 14 illustration physical principal of opposed phase imaging in neoplastic Lesion. Neoplastic lesion infiltrate the fatty marrow, so fat an water not is not equal, it will cause no signal suppression in opposed phase image

CASE 1
MULTIPLE MYELOMA

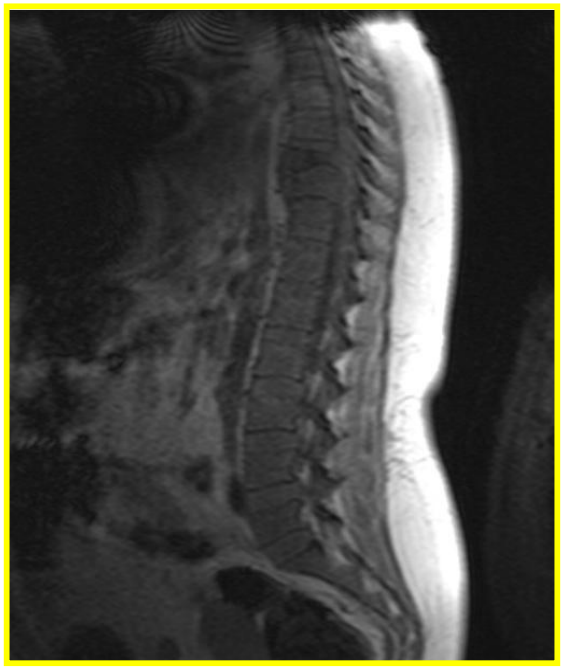


Fig15A Inphase image

Fig 15B Opposed phase image
Neoplastic lesion (multiple myeloma) of bone marrow shows no signal Suppression (hyperintense) in opposed phase image

CASE 2
APLASTIC ANEMIA

Fig 16A

Fig 16B

Fig16 A inphase image **FIG 16B** opposed phase image
on neoplastic lesion(marrow reconversion-red marrow) of bone marrow shows complete signal loss in opposed phase image

CASE 3

Carcinoma cervix with metastasis

Fig 17. Neoplastic lesion (metastasis) of bone marrow shows no signal Suppression (hyperintense) in opposed phaseimage. but Post radiotheraphy changes in L5 and sacrum also hyper intense in opposed phase image

Case 4
Metastaic adenocarcinoma

Fig 18.Neoplastic lesion (metastasis) of bone marrow shows no signal Suppression (hyper intense) in opposed phase image

Case 5
TB spondylitis

Fig 19. Opposed phase image of TB spondylitis . It shows no signal suppression in opposed phase image because infection also causes infiltration of fatty marrow

CASE 6

NHL (Non Hodgkins Lymphoma)

Fig 20.Neoplastic lesion (NHL) of bone marrow shows no signal Suppression (hyper intense) in opposed phase image

DISCUSSION:

Our results showed that in-phase and opposed of- phase spoiled gradient-echo MR Imaging was helpful in predicting the likelihood of neoplastic or non neoplastic signal abnormality in bone marrow. Visual assessment and expression of relative signal-intensity ratios were found to be of similar accuracy. we generated ROC curves that revealed 95% sensitivity and specificity for detection of neoplasm at a relative signal-intensity ratio cut off value of 0.82. No nonneoplastic lesion had a value greater than 0.96. and no neoplastic lesion had a value less than 0.86.Thus. for our patient group a cut off value between 0.82 would result in 100% sensitivity and 89.5% specificity for detection of neoplasm.

In-phase/opposed-phase imaging to assess for the presence of fat and water in a voxel of tissue has been used extensively in imaging of the liver and adrenal glands. The technique takes advantage of different precession frequencies of water and fat protons due to the differences in their molecular environment. Because they precess at slightly different frequencies, at 1.5T, water and fat protons are in phase with one another at a TE of 4.6 ms, and 180° opposed at a TE of 2.4 msec. This phenomenon is not usually evident on spin-echo sequences. Without a refocusing pulse, when there are both fat and water protons in a given

voxel, there will be some signal intensity loss on images that are obtained when the protons are in their opposed phase (TE _ 2.4 ms) . More signal intensity suppression occurs when the volume of fat and water is roughly equal. This technique is useful in identifying presence of fat coexistent with water in marrow lesions, thus predicting the likelihood of neoplasm in patients with marrow signal-intensity abnormalities. This likelihood is possible because most neoplastic lesions of bone marrow exist as solid masses with advancing fronts that completely destroy and replace all lipid and hematopoietic elements. whereas most nonneoplastic lesions (with the exception of tumour like lesions of bone such as bone cysts and fibrous dysplasia) do not exist as solid masses but rather as infiltrative hemorrhagic or inflammatory elements that comingle with, rather than replace, fat Signal that decreases in intensity on opposed phase compared with in-phase images indicates that fat and water are present in an area of marrow signal-intensity abnormality making neoplasm less likely. On the other hand. Signal intensity that does not decrease on opposed phase images indicates that fat and water are not coexistent. Making neoplasm more likely. Marrow dominated by fat also will not decrease in signal intensity on opposed phase images: however, the presence of fatty marrow is readily recognized by its high signal intensity on

conventional Tl weighted images . In this study. Tissues with significant signal contributions from both lipid and water (such as the cases of edema within avascular necrosis and fractures and normal and hyperplastic hematopoietic marrow) had cancellation of signal on the opposed phase images. resulting in decreased signal intensity compared with the in-phase images. On the other hand tissue dominated by water spins (such as the cases of metastases) showed little or no decrease in relative marrow signal intensity on the opposed phase images compared with the in-phase images.

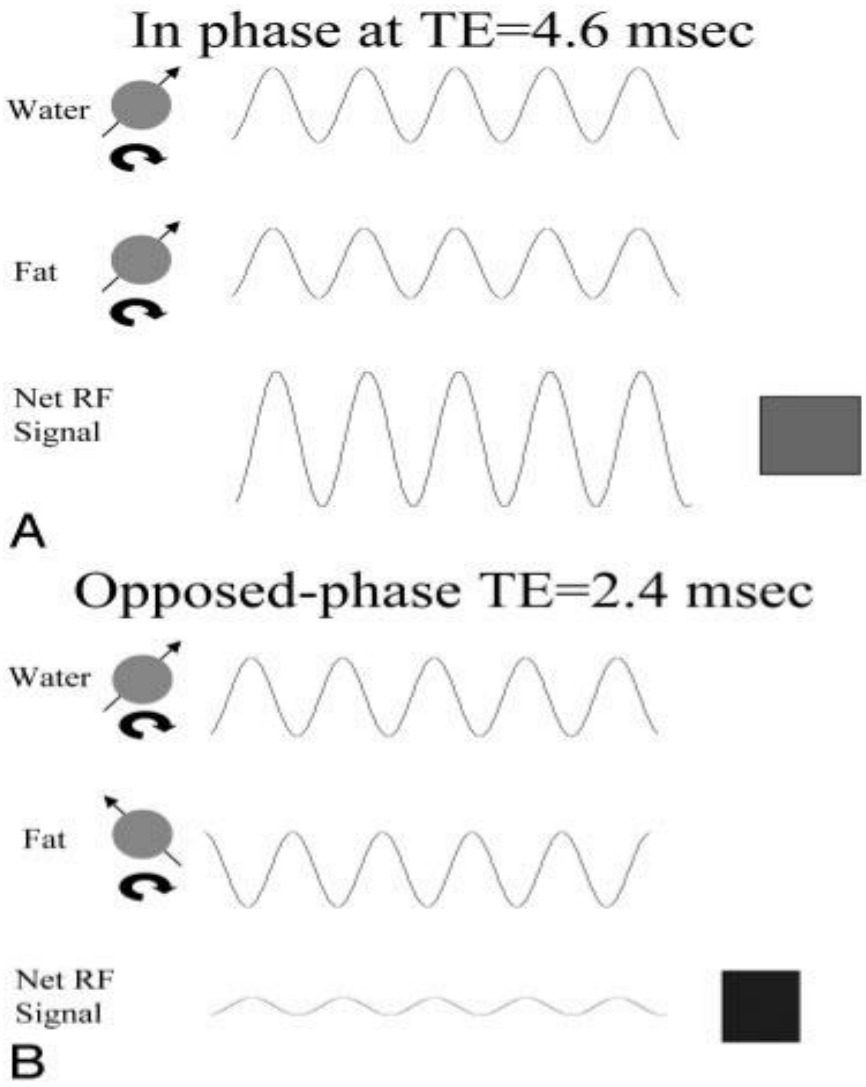


Fig 20 Illustration of the physical principles of in-phase/opposed-phase

A) Inphase B)Opposed phase

ADVANTAGES OF OPPOSED PHASE IMAGING:

i). A major advantage is that the technique can be performed rapidly. Imaging with in-phase and opposed phase imaging sequences adds at most 4-5 minutes to total imaging time.

ii). In addition. the techniques widely available: in-phase and opposed phase MR imaging is standard on most systems. .

iii). Because both quantitative and visual interpretation appear equally accurate for assessment of focal marrow abnormalities either can be used. Thus allowing for rapid interpretation from visual assessment.

iv) The potential clinical use of this technique for avoiding unnecessary biopsy

.v) It is also guiding tool for the biopsy

LIMITATIONS OF THE STUDY:

I) Two TB spondylitis lesion shows high relative signal intensity ratio (>0.8) signal intensity in TB spondylitis depending on the degree of infiltration of fatty marrow by inflammatory cellular elements and on whether abscess formation occurred.

ii) Some patients did not have direct pathologic correlation.

iii) Post radiotherapy shows lack of signal suppression in opposed phase image

iv) Only 38 patients were included in the study. This patient population may be small because a large variety of lesions can affect bone marrow. This results should be considered preliminary and in need of further evaluation. Future studies involving large patient groups may be helpful to determine the usefulness of this technique for specific marrow disorders.

CONCLUSION:

In-phase/opposed-phase imaging helpful in differentiating Neoplastic lesions from non neoplatic lesions of bone marrow. Furthermore, it may be an early indicator of response to treatment after radiation therapy to the spine .In-phase and opposed phase imaging sequences performed rapidly and just it adds only 4-5 minutes to total imaging time. In phase Opposed phase imaging has ability to demonstrate small amounts fat and fat- water mixture is the strongest advantage of this technique both quantitative and visual interpretation appear equally accurate for assessment of focal marrow abnormalities. either can be used. Thus allowing for rapid interpretation from visual assessment. TB spondylitis(non neoplastic lesion) included in this study shows high relative SIR . signal intensity in TB spondylitis depending on the degree of infiltration of fatty marrow by inflammatory cellular elements. So use of in phase opposed phase imaging in infection should be evaluated more.

In-phase/opposed-phase imaging is fast , most sensitive.Easly interpretable and useful sequence, in differentiating Neoplastic lesions from non neoplatic lesions of bone marrow.

BIBLIOGRAPHY

1. Siegel MJ. MR imaging of paediatric haematologic bone marrow disease. *J Hong Kong Coll Radiol* 2000; 3:38–50

2. Steiner RM, Mitchell DG, Rao VM, Schweitzer ME. Magnetic resonance imaging of diffuse bone marrow disease. *Radiol Clin North Am* 1993; 31: 383–409

3. Vande Berg BC, Malghem J, Lecouvet FE, Maldague B. Magnetic resonance imaging of the normal bone marrow. *Skeletal Radiol* 1998; 27:471–483

4. Vogler JB III, Murphy WA. Bone marrow imaging. *Radiology* 1998; 168:679–693

5. Eustace S, Tello R, DeCarvalho V, et al. A comparison of whole body turbo STIR MR imaging and planar 99mTc-methylene diphosphonate scintigraphy in the examination of patients with suspected skeletal metastases. *AJR* 1997; 169:1655–1661

6. Johnson KM, Leavitt GD, Kayser HWM. Total body MR imaging in as little as 18 seconds. *Radiology* 1997; 202:262–267

7. Layer G, Steudel A, Schuller H, et al. Magnetic resonance imaging to detect bone marrow metastases in the initial staging of small cell lung carcinoma and breast carcinoma. *Cancer* 1998; 85:1004–1009

8. Lauerstein TC, Goedhe SC, Herborn CU, et al. Three-dimensional volumetric interpolated breath-hold MR imaging for whole-body tumor staging in less than 15 minutes: a feasibility study. *AJR* 2002; 179:445–449

9. Lauerstein TC, Goedhe SC, Herborn CU, et al. Whole-body MR imaging: evaluation of patients for metastases. *Radiology* 2004; 233:139–148

10. Mazumdar A, Siegel M, Narra V, Luchtman-Jones L. Whole-body fast inversion recovery MR imaging of small cell neoplasms in pediatric patients: a pilot study. *AJR* 2002; 179:1261–1266

11. O'Connell MJ, Hargaden G, Powell T, Eustace SJ. Whole-body short tau inversion recovery MR imaging with a moving table top. *AJR* 2002; 179:866– 868

12. Takahara T, Imai Y, Yamashita T, et al. Diffusion weighted whole body imaging with background body signal suppression (DWIBS): technical improvement using free breathing STIR and high resolution 3D display. *Radiat Med* 2004; 22:275–282

13. Jones KM, Unger EC, Granstom P, Seeger JF, Carmody RF, Yoshino M. Bone marrow imaging using STIR at 0.5 and 1.5T. *Magneson Imaging* 1992; 10:169–176

14. Padhani A, Husband J. Bone. In: Husband JES, Reznek RH, eds. *Imaging in oncology.* Oxford: Isis Medical Media, 1998:765–786

15. Kricun ME. Red-yellow marrow conversion: its effect on the location of some solitary bone lesions. *Skeletal Radiol* 1985; 14:10–19

16. Custer RP, Ahlfeldt FE. Studies of the structure and function of bone marrow: variations in cellularity in various bones with advancing years of life and their relative response to stimuli. *J Lab Clin Med* 1932;17:960–962

17. Dawson KL, Moore SG, Rowland JM. Age-related marrow changes in the pelvis: MR and anatomic findings. *Radiology* 1992; 183:47–51

18. Moore DG, Dawson KL. Red and yellow marrow in the femur: age-related changes in the appearance at MR imaging. *Radiology* 1990; 175:219–223

19. Ricci C, Cova M, Kang YS, et al. Normal age-related patterns of cellular and fatty bone marrow distribution in the axial skeleton: MR imaging study. *Radiology* 1990; 177:83–88

20. Taccone A, Oddone M, Dell' Acqua A, Occhi M, Ciccone MA. MRI "roadmap" of normal age-related bone marrow. *Pediatr Radiol* 1995; 25:596–606

21. Waitches G, Zawin JK, Poznanski AK. Sequence and rate of bone marrow conversion in the femora of children as seen on MR imaging: are accepted standards accurate? *AJR* 1994; 162:1399–1406

22. Zawin JK, Jaramillo D. Conversion of bone marrow in the humerus, sternum,and clavicle: changes with age on MR images. *Radiology* 1993; 188:158–164

23. Mirowitz SA. Hematopoietic bone marrow within the proximal humeral epiphysis in normal adults: investigation with MR imaging. *Radiology* 1993; 188:689–693

24. Fletcher BD, Wall JE, Hanna SL. Effect of hematopoietic growth factors on MR images of bone marrow in children undergoing chemotherapy. *Radiology* 1993; 189:745–751

25. Ryan SP, Weinberger E, White KS, et al. MR imaging of bone marrow in children with osteosarcoma: effect of granulocyte colony-stimulating factor. *AJR* 1995; 165:915–920

26. Shellock FG, Morris E, Deutsch AL, et al. Hematopoietic bone marrow hyperplasia: high prevalence on MR images of the knee in asymptomatic marathon runners. *AJR* 1992; 158:335–338

27. Siegel MJ. Leukemia. In: Siegel BA, Choplin RH, Siegel MJ, Stephens DH, eds. *Body MRI test and syllabus.* Reston, VA: American College of Radiology, 2000:173–189

28. Morrison WB, Schweitzer ME, Bock GW, et al. Diagnosis of osteomyelitis: utility of fat-suppressed contrast-enhanced MR imaging. *Radiology* 1993; 189:251–257

29. Baker LL, Goodman SB, Perkash I, Lane B, Enzmann DR. Benign versus pathologic compression fractures of vertebral bodies: assessment with conventional spin-echo, chemical shift, and STIR MR imaging. *Radiology* 1990; 174:495–502

30. Kaplan PA, Asleson RJ, Klassen LW, Duggan MJ. Bone marrow patterns in aplastic anemia: observations with 1.5-T MR imaging. *Radiology* 1987; 164:441–444

31. McKinstry CS, Steiner RE, Young AT, Jones L, Swirsky D, Aber V. Bone marrow in leukemia and aplastic anemia: MR imaging before, during, and after treatment. *Radiology* 1987; 162:701–707

32. Blomlie V, Rofstad EK, Skjonsberg A, Tverå, Lien HH. Female pelvic bone marrow: serial MR imaging before, during, and after radiation therapy. *Radiology* 1995; 194:537–543

33. Stevens SK, Moore SG, Kaplan ID. Early and late bone-marrow changes after irradiation: MR evaluation. *AJR* 1990; 154:745–750

34. Yankelevitz DF, Henschke CI, Knapp PH, Nisce L, Yi Y, Cahill P. Effect of radiation therapy on thoracic and lumbar bone marrow: evaluation with MR imaging. *AJR* 1991; 157:87–92

35. Otake S, Mayr N, Ueda T, et al. Radiation-induced changes in the MR signaland contrast enhancement of lumbosacral vertebrae: do changes occur only inside the radiation therapy field? *Radiology* 2002; 222:179– 183

36. Hermann G, Shapiro RS, Abdelwahab IF, Grabowksi G. MR imaging in adults with Gaucher disease type I: evaluation of marrow involvement and disease activity. *Skeletal Radiol* 1993; 22:247–251

37. Levin TL, Sheth SS, Hurlet A, et al. MR marrow signs of iron overload in transfusion-dependent patients with sickle cell disease. *Pediatr Radiol* 1995; 25:614–619f

38. Disler DG, McCauley TR, Ratner LM, et al. In-phase and out-of-phase MR imaging of bone marrow: prediction of neoplasia based on the detection of coexistent fat and water. *AJR Am J Roentgenol* 1997;169:1439–47

39. W.K. Erly E.S. OhE.K. Outwater et al. The Utility of In-Phase/ Opposed-Phase Imaging in Differentiating Malignancy from Acute Benign Compression Fractures of the Spine AJNR Am J Neuroradiol 27:1183– 88 _ Jun-Jul 2006 _

INPHASE OPPOSED IMAGING OF BONE MARROW

DIFFERENTIATING NEOPLASTIC LESIONS FROM

NON NEOPLASTIC LESION

PROFORMA

NAME: AGE/ SEX : STUDY NO:

ADDRESS

PHONE NO

CLINICAL HISTORY:

PAST HISTORY:

RISK FACTORS:

	Inphase image			Opposed phase image			Relative SIR	Diagnosis	Biopsy
	SIR of lesion	SIR of controlsite	SIR of inphase image	SIR of lesion	SIR of control site	SIR of opposed phase image			

Consent Form

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு

எலும்பு மஜ்ஜை நோய்களை காந்த கதிர்வலை கருவிமூலம் கண்டு அறிதல்

பார்ணார்டு நுண் கதிரியல் துறை : அரசு பொது மருத்துவமனை, சென்னை

பங்கு பெறுபவரின் பெயர் :

பங்கு பெறுபவரின் எண் :

பங்கு பெறுவர் இதனை (✔) குறிக்கவும் :

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன். ( )

நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்தும் கொண்டேன். ( )

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். ( )

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்கமாட்டேன். ( )

இந்த ஆய்வில் பங்குகொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாரோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ( )

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி
ஆய்வாளரின் பெயர் .....

ABBERVIATIONS:

ALL - Acute Lympocytic Leukemia

CLL - Chronic Lymphocytic Leukemia

MRI - Magnetic Resonance Imaging

NHL - Non Hodgkins Lympoma

GRE - Gradient Recalled Echo

ROC – Receiver Operating Characteristic Curve

SIR - Signal Intensity Ratio

STIR - Short Time of Inversion Recovery

TR - Time of Repetition

TE - Time of Echo

SNO	NAME	AGE	SEX	BONE MARROW DISORDERS	RELA-TIVE SIR
23	mari	42	M	TB spondylitis	0.90
24	Abdul reh-man	43	M	Hyperplastic red marrow	0.42
25	arunkumar	18	M	Hemosiderotic marrow	0.38
26	Peula	36	F	Avascular necrosis	0.56
27	kamala	52	F	Traumatic fracture	0.60
28	selvi	47	F	TB spondylitis	0.96
29	muthukumar	17	M	Aplastic anemia	0.48
30	kavitha	25	F	Hyperplastic red marrow	0.50
31	ponnusamy	62	M	Traumatic fracture	0.67
32	gajendran	41	M	TB spondylitis	0.78
33	janaki	37	F	Bone infarct	0.51
34	thiyagarajan	22	M	Hyperplatic red marrow	0.52
35	periyasamy	64	M	Traumatic fracture	0.62
36	priya	32	F	Avascular necrosis	0.54
37	arumugam	67	M	Traumatic fracture	0.68
38	rajendran	23	M	Aplstic anemia	0.50

MASTER CHART

SNO	NAME	AGE	SEX	BONE MARROW DISORDERS	RELA-TIVE SIR
1	shanmugam	65	M	Multiple myeloma	1.2
2	murugan	62	M	Multiple myeloma	1.1
3	palani	45	M	NHL	1.26
4	swetha	14	F	ALL	1.06
5	kumari	56	F	metastasis	1.08
6	rajamani	49	F	metastasis	0.92
7	raja	55	M	CLL	1.2
8	kandasamy	58	M	Metastasis	1.1
9	anand	13	M	ALL	1.02
10	rajammal	45	F	Metastasis	0.98
11	kala	34	F	NHL	1.1
12	krishnan	15	M	ALL	1
13	prabhu	11	F	ALL	1.2
14	jegathammal	68	F	Metastasis	0.98
15	kannan	42	M	NHL	1.1
16	ramasamy	64	M	Multiple myeloma	0.86
17	saroja	51	F	metastasis	0.88
18	kalaiselvi	57	M	Multiple myeloma	1.2
19	ramayee	65	F	Metastasis	1.3
20	pandian	24	M	Traumatic fracture	0.76
21	chellammal	34	F	Bone infarct	0.60
22	kandhan	46	F	Traumatic fracture	0.70